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Amendments to the Specification

On page 1, please replace the paragraph beginning on line 5 with the following amended paragraph:

-- This application is a continuation of ~~Continued Prosecution Application Serial No. 08/986,016 filed on November 17, 2000, which is a continuation of~~ U.S. Patent Application Serial No. 08/986,016 filed on December 5, 1997, now abandoned. --

Please replace the paragraph beginning at line 26 on page 10 with the following amended paragraph:

-- FIGURES 2a and 2b show the amino acid sequences of V_λ (SEQ ID NO: 44) and V_κ (SEQ ID NO: 45), respectively, of mouse monoclonal antibody LM609. The N-terminal two amino acids (Leu)(Glu) of V and (Glu)(Leu) of V encoded by the vector cloning sites CTCGAG (XhoI) and GAGCTC (SacI), respectively, are artificial. The CDR loops are underlined. --

On page 11, between lines 7 and 8, please insert the following new paragraphs:

-- In FIGURE 3a, the top line (labeled "V_κ") represents amino acid residues 5-23 of SEQ ID NO: 45. The lines labeled " #1" and " #3" each represent amino acid residues of human V_κ clones having Ser in alignment with Thr7 of SEQ ID NO: 45, Gly-Thr in alignment with Ala9-Thr10 of SEQ ID NO: 45, Leu-Ser in alignment with Val13-Thr14 of SEQ ID NO: 45, and Glu-Arg-Ala-Thr (SEQ ID NO: 57) in alignment with Asp17-Ser18-Val19-Ser20 of SEQ ID NO: 45. The line labeled " #2" represents amino acid residues of a human V_κ clone having Ser in alignment with Thr7 of SEQ ID NO: 45, Gly-Thr in alignment with Ala9-Thr10 of SEQ ID NO: 45, Leu-Ser in alignment with Val13-Thr14 of SEQ ID NO: 45, and Glu-Arg-Gly-Ser (SEQ ID NO: 58) in alignment with Asp17-Ser18-Val19-Ser20 of SEQ ID NO: 45. The lines labeled " #4" and " #6" each represent amino acid residues of a human V_κ clone having Ser in alignment with Thr7 of SEQ ID NO: 45, Ser-Ser in alignment with

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Ala9-Thr10 of SEQ ID NO: 45, Ala-Ser-Val in alignment with Val13-Thr14-Pro15 of SEQ ID NO: 45, Arg in alignment with Ser18 of SEQ ID NO: 45, and Thr-Ile-Thr in alignment with Ser20-Leu21-Ser22 of SEQ ID NO: 45. The line labeled " #5" represents amino acid residues of a human V_κ clone having Ser in alignment with Thr7 of SEQ ID NO: 45, Ser-Ser in alignment with Ala9-Thr10 of SEQ ID NO: 45, Ala-Ser-Val in alignment with Val13-Thr14-Pro15 of SEQ ID NO: 45, and Thr-Ile-Thr in alignment with Ser20-Leu21-Ser22 of SEQ ID NO: 45. --

-- In FIGURE 3b, the top line (labeled "V_κ") represents amino acid residues 24-34 of SEQ ID NO: 45. The line labeled " #1" represents amino acid residues of a human V_κ clone having Val in alignment with Ile29 of SEQ ID NO: 45, and Ser-Ser-Thr-Leu-Ala (SEQ ID NO: 59) in alignment with Asn31-His32-Leu33-His34 of SEQ ID NO: 45. The line labeled " #2" represents amino acid residues of a human V_κ clone having Val in alignment with Ile29 of SEQ ID NO: 45, and Ser-Ser-Phe-Leu-Ala (SEQ ID NO: 60) in alignment with Asn31-His32-Leu33-His34 of SEQ ID NO: 45. The line labeled " #3" represents amino acid residues of a human V_κ clone having Val-Thr-Ser-Ser-Tyr-Leu-Ala (SEQ ID NO: 61) in alignment with Ile29-Ser30-Asn31-His32-Leu33-His34 of SEQ ID NO: 45. The line labeled " #4" represents amino acid residues of a human V_κ clone having Thr-Phe in alignment with Asn31-His32 of SEQ ID NO: 45, and Asn in alignment with His34 of SEQ ID NO: 45. The lines labeled " #5" and " #6" each represent amino acid residues of human V_κ clones having Ser-Tyr in alignment with Asn31-His32 of SEQ ID NO: 45, and Asn in alignment with His34 of SEQ ID NO: 45. --

-- In FIGURE 3c, the top line (labeled "V_κ") represents amino acid residues 35-49 of SEQ ID NO: 45. The lines labeled " #1", " #2", and " #3" each represent amino acid residues of human V_κ clones having Pro-Gly-Gln-Ala (SEQ ID NO: 62) in alignment with Ser40-His41-Glu42-Ser43 of SEQ ID NO: 45 and Tyr in alignment with Lys49 of SEQ ID NO: 45. The line labeled " #4" represents amino acid residues of a human V_κ clone having Pro-Gly-Lys-Ala (SEQ ID NO: 63) in alignment with Ser40-His41-Glu42-Ser43 of SEQ ID NO: 45, Lys-Phe in alignment with Arg45-Leu46 of SEQ ID NO: 45, and Tyr in alignment with Lys49 of SEQ ID NO: 45. The line labeled " #5" represents amino acid residues of a human V_κ clone

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having Arg in alignment with Gln38 of SEQ ID NO: 45, Pro-Gly-Lys-Ala (SEQ ID NO: 63) in alignment with Ser40-His41-Glu42-Ser43 of SEQ ID NO: 45, Lys-Leu in alignment with Arg45-Leu46 of SEQ ID NO: 45, and Tyr in alignment with Lys49 of SEQ ID NO: 45. The line labeled " #6" represents amino acid residues of a human V_κ clone having Pro-Gly-Lys-Ala (SEQ ID NO: 63) in alignment with Ser40-His41-Glu42-Ser43 of SEQ ID NO: 45, Lys-Leu in alignment with Arg45-Leu46 of SEQ ID NO: 45, and Tyr in alignment with Lys49 of SEQ ID NO: 45. --

-- In FIGURE 3d, the top line (labeled "V_κ") represents amino acid residues 50-56 of SEQ ID NO: 45. The lines labeled " #1", " #2", and " #3" each represent amino acid residues of human V_κ clones having Gly in alignment with Tyr50 of SEQ ID NO: 45, and Ser-Arg-Ala-Thr (SEQ ID NO: 64) in alignment with Gln53-Ser54-Ile55-Ser56 of SEQ ID NO: 45. The lines labeled " #4", " #5" and " #6" each represent amino acid residues of human V_κ clones having Ala in alignment with Tyr50 of SEQ ID NO: 45, and Thr-Leu-Gln in alignment with Gln53-Ser54-Ile55 of SEQ ID NO: 45. --

-- In FIGURE 3e, the top 2 lines (labeled "V_κ") represent amino acid residues 57-88 of SEQ ID NO: 45. The lines labeled " #1" represent amino acid residues of a human V_κ clone having Asp in alignment with Ser60 of SEQ ID NO: 45, Ile in alignment with Thr72 of SEQ ID NO: 45, Thr in alignment with Ser74 of SEQ ID NO: 45, Ser-Arg-Leu in alignment with Asn76-Ser77-Val78 of SEQ ID NO: 45, Pro in alignment with Thr80 of SEQ ID NO: 45, Ala-Val in alignment with Gly84-Met85 of SEQ ID NO: 45, and Tyr in alignment with Phe87 of SEQ ID NO: 45. The lines labeled " #2" represent amino acid residues of a human V_κ clone having Asp in alignment with Ser60 of SEQ ID NO: 45, Val in alignment with Asp70 of SEQ ID NO: 45, Thr in alignment with Ser74 of SEQ ID NO: 45, Ser-Arg-Leu in alignment with Asn76-Ser77-Val78 of SEQ ID NO: 45, Pro in alignment with Thr80 of SEQ ID NO: 45, Ala-Val in alignment with Gly84-Met85 of SEQ ID NO: 45, and Tyr in alignment with Phe87 of SEQ ID NO: 45. The lines labeled " #3" represent amino acid residues of a human V_κ clone having Asp in alignment with Ser60 of SEQ ID NO: 45, Ile-Phe-Thr in alignment with Thr72-Leu73-Ser74 of SEQ ID NO: 45, Ser-Arg-Leu in alignment with Asn76-Ser77-Val78 of SEQ ID NO: 45, Pro in alignment with Thr80 of

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SEQ ID NO: 45, Ala-Val in alignment with Gly84-Met85 of SEQ ID NO: 45, and Tyr in alignment with Phe87 of SEQ ID NO: 45. The lines labeled " #4" and " #6" each represent amino acid residues of human V_κ clones having Val in alignment with Ile58 of SEQ ID NO: 45, Thr in alignment with Ser74 of SEQ ID NO: 45, Ser in alignment with Asn76 of SEQ ID NO: 45, Leu-Gln-Pro in alignment with Val78-Glu79-Thr80 of SEQ ID NO: 45, Ala-Val in alignment with Gly84-Met85 of SEQ ID NO: 45, and Tyr in alignment with Phe87 of SEQ ID NO: 45. The lines labeled " #5" represent amino acid residues of a human V_κ clone having Val in alignment with Ile58 of SEQ ID NO: 45, Ala in alignment with Gly68 of SEQ ID NO: 45, Thr in alignment with Ser74 of SEQ ID NO: 45, Ser in alignment with Asn76 of SEQ ID NO: 45, Leu-Gln-Pro in alignment with Val78-Glu79-Thr80 of SEQ ID NO: 45, Ala-Val in alignment with Gly84-Met85 of SEQ ID NO: 45, and Tyr in alignment with Phe87 of SEQ ID NO: 45. --

On page 11, between lines 11 and 12, please insert the following new paragraph:

-- In FIGURE 4, the top sequence line shows portions of the mouse LCDR1 and LCDR2 loops, i.e., Arg-Ala-Ser-Gln-Ser-Ile-Ser-Asn (SEQ ID NO: 65) and His-Leu-His in the LCDR1 loop, and Lys-Tyr-Ala-Ser-Gln-Ser-Ile-Ser (SEQ ID NO: 66) in the LCDR2 loop. The second sequence line shows a selected human sequence in which a first portion (SEQ ID NO: 67) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Ser-Leu-His) in alignment with His-Leu-His in the mouse LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 68. The third sequence line shows a selected human sequence in which a first portion (SEQ ID NO: 69) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Ser-Leu-His) in alignment with His-Leu-His in the mouse LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 68. The fourth sequence line shows a selected human sequence in which a first portion (SEQ ID NO: 70) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Ser-Leu-His) in alignment with His-Leu-His in the mouse LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 71. The fifth sequence line shows an unselected human sequence in which a first portion (SEQ ID NO: 72) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Thr-Leu-Ala) in alignment with His-Leu-His in the mouse

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LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 73. The sixth sequence line shows an unselected human sequence in which a first portion (SEQ ID NO: 74) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Thr-Leu-Ala) in alignment with His-Leu-His in the mouse LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 75. The seventh sequence line shows an unselected human sequence in which a first portion (SEQ ID NO: 76) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Thr-Leu-Ala) in alignment with His-Leu-His in the mouse LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 77. The eighth sequence line shows an unselected human sequence in which a first portion (SEQ ID NO: 78) is in alignment with SEQ ID NO: 65 of the mouse LCDR1 loop, a second portion (Thr-Leu-Ala) in alignment with His-Leu-His in the mouse LCDR1 loop, and the LCDR2 loop comprises SEQ ID NO: 79. --

Please replace the paragraph beginning at line 28 on page 11 with following amended paragraph:

-- FIGURE 7 is a schematic illustration of a stretch of four amino acids in a light chain complementarity determining region three (LCDR3) and a heavy chain complementarity determining region three (HCDR3) being optimized. In FIGURE 7, QQSNSWPHT is SEQ ID NO: 2, HNYGSFAY is SEQ ID NO: 1, QQXXXXPHT is SEQ ID NO: 121, and XXXXSFAY is SEQ ID NO: 122. --

Please replace the paragraph beginning at line 33 on page 11 with following amended paragraph:

-- FIGURES 8a and 8b are fragmented illustrations of the V_L amino acid sequences of a mouse antibody compared to the amino acid sequences of five versions of humanized clones represented by group letters A (clones 10, 11, and 37), and B (clones 7, 8, and 22), C (clones 4, 31, and 36), D (clones 24, 34, 35, and 40), and E (clone 2) which are combined. In FIGURE 8a, the mouse FR1 region is SEQ ID NO: 80; the human Group A and Group BCDE FR1 regions are each SEQ ID NO: 81; the mouse CDR1 region is SEQ ID NO: 82;

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the human Group A CDR1 region is SEQ ID NO: 83; the human Group BCDE CDR1 regions are each SEQ ID NO: 84; the mouse FR2 region is SEQ ID NO: 85; the human Group A and Group BCDE FR2 regions are each SEQ ID NO: 86; the mouse CDR2 region is SEQ ID NO: 87; and the human Group A and Group BCDE CDR2 regions are each SEQ ID NO: 88. In FIGURE 8b, the mouse FR3 region is SEQ ID NO: 89; the human Group A FR3 region is SEQ ID NO: 90; the human Group BCDE FR3 regions are each SEQ ID NO: 91; the mouse CDR3 region, as well as the human Group A and human Group BCDE CDR3 regions, are each SEQ ID NO: 92; the mouse FR4 region is SEQ ID NO: 92; while the human Group A and human Group BCDE FR4 regions are each SEQ ID NO: 93. --

On page 12, after line 12, please add the following new paragraphs;

-- In FIGURE 8c, the mouse FR1 region is SEQ ID NO: 94; the human Group A FR1 region is SEQ ID NO: 95; the human Group B FR1 region is SEQ ID NO: 96; the human Group C FR1 region is SEQ ID NO: 97; the human Group D FR1 region is SEQ ID NO: 98; the human Group E FR1 region is SEQ ID NO: 99; the mouse CDR1 region is SEQ ID NO: 100; the human Group A CDR1 region is SEQ ID NO: 101; the human Group B CDR1 region is SEQ ID NO: 102; the human Group C, D, and E CDR1 regions are each SEQ ID NO: 103; the mouse FR2 region is SEQ ID NO: 104; the human Group A FR2 region is SEQ ID NO: 105; the human Group B FR2 region is SEQ ID NO: 106; the human Group C and E FR2 regions are each SEQ ID NO: 107; and the human Group D FR2 region is SEQ ID NO: 108. --

-- In FIGURE 8d, the mouse CDR2 region is SEQ ID NO: 108; the human Group A CDR2 region is SEQ ID NO: 109; the human Group B CDR2 region is SEQ ID NO: 110; the human Group C CDR2 region is SEQ ID NO: 111; the human Group D and Group E CDR2 regions are both SEQ ID NO: 112; the mouse FR3 region is SEQ ID NO: 113; the human Group A FR3 region is SEQ ID NO: 114; the human Group B FR3 region is SEQ ID NO: 115; the human Group C FR3 region is SEQ ID NO: 116; the human Group D FR3 region is SEQ ID NO: 117; and the human Group E FR3 region is SEQ ID NO: 118. --

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-- In FIGURE 8e, the mouse CDR3 region, as well as the human Group A, B, C, D and E CDR3 regions are each SEQ ID NO: 1; the mouse FR2 region is SEQ ID NO: 119, while the human Group A, B, C, D, and E FR2 regions are each SEQ ID NO: 120. --

Please replace the paragraph beginning at line 25 on page 12 with the following amended paragraph:

-- Beginning with a LM609 hybridoma cell line (Deposited at and accepted by American Type Culture Collection, ~~12301 Parklawn Drive, Rockville, MD 20852-1776~~ 10801 University Boulevard, Manassas, VA 20110-2209, USA on September, 15, 1987; ATCC Designation HB 9537), total RNA was prepared from 10^8 LM609 hybridoma cells using an RNA Isolation Kit (Stratagene, La Jolla, CA). Reverse transcription and polymerase chain reaction (PCR) amplification of Fd fragment and κ chain encoding sequences were performed essentially as described in "Combinatorial immunoglobulin libraries in phage I", (*Methods* **2**, 119 (1991)) by A.S. Kang, et al. --